THE IMPORTANCE OF RETINAL FINDINGS IN ESSENTIAL HYPERTENSION*

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IN judging the severity and prognosis of hypertensive cardiovascular disease, no examination, including measurement of blood pressure, is more important than careful ophthalmoscopy.

KEITH-WAGENER-BARKER CLASSIFICATION

In 1939 Keith, Wagener, and Barker[1] drew attention to the prognostic significance of ophthalmoscopic findings in hypertensive patients, and they outlined criteria for classifying hypertensive disease into four groups according to the severity of retinal changes (Table I). The grouping depends entirely on ophthalmoscopic findings and excludes consideration of the level of blood pressure and the presence or absence of complications.

The term "hypertensive angiopathy" refers to pathologic changes (narrowing and sclerosis) confined to the retinal arterioles in the absence of hemorrhages, exudates, or papilledema; "hypertensive retinopathy" refers to the presence of hemorrhages and exudates in addition to arteriolar abnormalities; "hypertensive neuroretinopathy" is reserved for the presence of papilledema (Group 4).

The distinguishing feature between Keith-Wagener-Barker Groups 1 and 2 is the presence of arteriolosclerosis in Group 2 (Table I), irrespective of the severity of generalized or focal narrowing of the arterioles. The presence of exudates is the characteristic feature of Keith-Wagener-Barker Group 3, whereas papilledema is the pathognomonic feature of Group 4 or malignant hypertension.

In their original description, Keith, Wagener, and Barker[1] included in Group 2 those patients who, in addition to having angiopathy, had retinal hemorrhages without exudates and papilledema. A more recent

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TABLE I. OPHTHALMOSCOPIC CLASSIFICATION OF HYPERTENSION ACCORDING TO KEITH, WAGENER, AND BARKER[1]

	Retinal Arterioles					
K-W-B group	*Sclerosis grade**	*General narrowing† grade*	*Focal narrowing‡ grade*	*Hemorrhages*	*Exudates*	*Papilledema*
1	< 1	0-4	0-4	—§	—	—
2	1 or more	0-4	0-4	±	—	—
3	0-4	0-4	0-4	±	+	—
4	0-4	0-4	0-4	±	±	+

*Grading of sclerosis: 1) brightening or increased luster of arterioles, mild depression of veins at points of arteriolar crossing with reduction in visibility of those portions of veins that underlie crossing arterioles; 2) burnished coppery color of arterioles with definite depression of underlying veins, widening of apparent arteriolovenous crossing spaces, and almost complete invisibility of portions of veins underlying crossing arterioles; 3) polished silver color of arterioles, widening of apparent arteriolovenous crossing spaces with change in course of veins ("right-angled crossings"), complete invisibility of portions of veins underlying crossing arterioles, and distal dilatation of veins; and 4) arterioles visible only as fibrous cords without a bloodstream.

†Grading of generalized narrowing: 1) reduction of caliber of arterioles to three-fourths average caliber or one-half caliber of veins; 2) reduction of caliber of arterioles to one-half average caliber or one-third caliber of veins; 3) reduction of caliber of arterioles to one-third average caliber or one-fourth caliber of veins; and 4) arterioles threadlike or invisible.

‡Grading of focal narrowing: 1) localized narrowing to two-thirds caliber of proximal segment of arteriole; 2) localized narrowing to one-half caliber of proximal segment of arteriole; 3) localized narrowing to one-third caliber of proximal segment of arteriole; and 4) arteriole invisible beyond point of constriction (or, in case of focal sclerosis, visible only as a thin, fibrous cord).

§The symbol + signifies presence, – signifies absence, and ± signifies either presence or absence.
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study of the natural history of hypertension by Breslin and his colleagues[2] demonstrated that patients who have hemorrhages without retinal exudates have an intermediate prognosis between that of patients with Group 2 angiopathy (without hemorrhages) and of patients with Group 3 retinopathy (exudates with or without hemorrhages). Consequently I have assigned to these patients the classification of Group 2+. In contrast, when retinal hemorrhages are confined to one segment of the retina and are associated with thrombosis in the arteriole or vein that supplies that region, the prognosis is no worse than that for other patients with Group 2 hypertensive angiopathy.[2]

Although data presented here have largely been derived from patients with essential hypertension, the findings are equally valid and have the same connotation for patients with hypertension from any cause.

SIGNIFICANCE OF ARTERIOLAR NARROWING

The terms "constriction" and "narrowing" of the retinal arterioles are synonomous and describe a reversible state of spasm of the arterioles

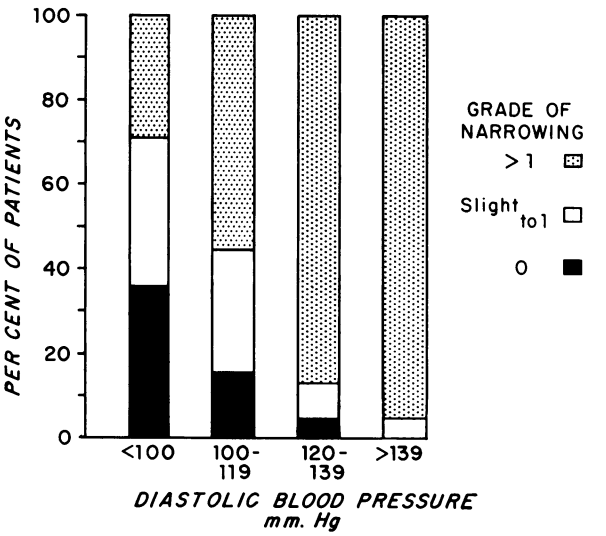

Fig. 1. Relation between generalized retinal arteriolar narrowing and diastolic blood pressure in patients with essential hypertension. Reproduced by permission of the *Journal of the American Medical Association.*[2]

which may be generalized or focal or both. The severity of arteriolar narrowing, both focal and generalized, can be graded quantitatively according to criteria outlined in 1947 by a committee[3] of the American Ophthalmological Society, whose chairman was the late Henry Wagener (Table I). The severity of both types of arteriolar narrowing is closely correlated with severity of diastolic hypertension[2] (Figures 1 and 2). It is unusual for a patient with sustained diastolic blood pressure of 120 mm. Hg or higher not to have some degree of generalized arteriolar narrowing, whereas patients with minimally elevated diastolic blood pressures often have little or no generalized narrowing of retinal arterioles. This fact is helpful in the initial study of patients who have labile hypertension with spuriously high diastolic levels at the first examination. I have found that patients whose diastolic blood pressure is in the range of 125 mm. Hg or higher when it is first measured, but who have little or no arteriolar narrowing, almost inevitably have much lower blood pressures on subsequent examinations or when they are hospitalized.

Focal narrowing of retinal arterioles also correlates well with severity of diastolic hypertension (Figure 2), but in addition usually signifies recent onset or exacerbation of hypertension. It is frequently

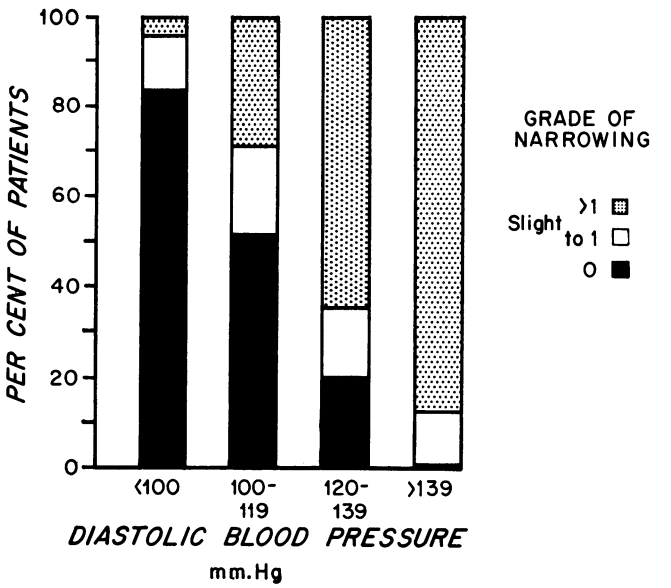

Fig. 2. Relation between focal narrowing of retinal arterioles and diastolic blood pressure in patients with essential hypertension. Reproduced by permission of the *Journal of the American Medical Association.*[2]

associated with accelerated hypertension and is objective confirmation of a short history or a recent worsening of hypertension. Angiospastic retinopathy" is characterized by severe focal narrowing of retinal arterioles (usually with generalized narrowing as well, but with little or no sclerosis) in addition to hemorrhages and exudates with or without papilledema. It signifies active disease and often is found in association with occlusive disease of the renal artery or with pheochromocytoma.

Significance of Arteriolosclerosis

Although it is difficult to document, it is my clinical impression that sclerosis of retinal arterioles as manifested by increase in light reflex and arteriovenous nicking[3] (Table I) is more closely related to duration of hypertension than to its severity. The presence of advanced sclerosis argues against recent onset of hypertension. Whether or not sclerosis of retinal arterioles occurs in the absence of hypertension has been a moot point among ophthalmologists. While sclerotic changes are sometimes observed in the retinal arterioles of elderly, normotensive individuals, it is frequently difficult to prove that they have not been hypertensive in the past.

In contrast to generalized and focal narrowing of arterioles which represents reversible spasm that abates when blood pressure is reduced by appropriate treatment, sclerosis is an organic change in the wall of the arteriole, which regresses little if any when blood pressure is reduced.[4, 5]

Significance of Hypertensive Retinopathy

"Cotton-wool" or soft exudates in the retinas of hypertensive patients are associated with increased permeability of capillaries, probably as a result of vascular damage from severe hypertension and ischemia.[6] Microscopically, exudates appear as localized lenticular swellings of the retinal nerve fiber layer containing edema fluid (presumably an exudate as opposed to a transudate), amorphous fibrinoid material, intact nerve fibers, and cytoid bodies.[7, 8] Retinal exudates are associated with acceleration of hypertension and usually reflect widespread vascular damage. Eighty per cent of soft exudates are intimately associated with vascular lesions, usually capillary microaneurysms, although fluorescent angiography is often required to demonstrate microaneurysms in nondiabetic patients.[6]

In addition to the soft, fluffy, cotton-wool exudates, some patients with severe diastolic hypertension have punctate, more deeply placed exudates called "edema residues." Frequently these punctate exudates are arranged radially, like spokes of a wheel, with the macula at the center, a configuration known as a "macular star" or "star figure." In the course of hypertension, punctate exudates usually appear later than the cotton-wool exudates, and the finding of a macular star usually connotes subsiding malignant hypertension.[3, 6] Both types of exudate regularly regress and ultimately disappear when blood pressure is reduced.[4, 5]

Significance of Neuroretinopathy

Papilledema is the distinguishing feature of Group 4 or malignant hypertension, so called because of its grave prognostic implications. Only rarely does papilledema secondary to hypertension occur in the absence of retinal hemorrhages and exudates and, when it does, an intracranial lesion should be carefully excluded. Severe arteriolar narrowing, both generalized and focal, is usually present by the time papilledema appears. The pathogenesis of papilledema associated with hypertension is not clear, because not all patients with malignant hypertension have

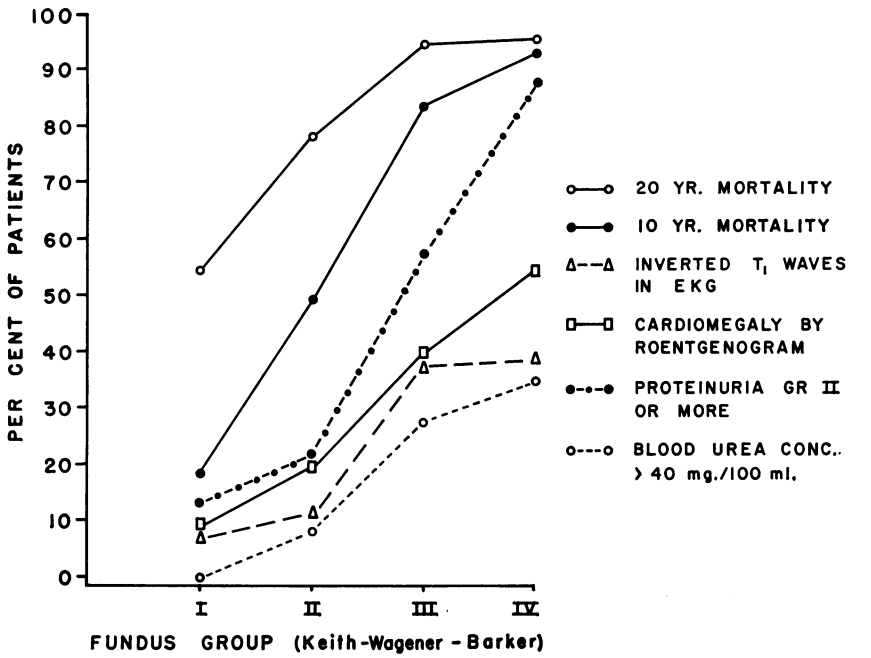

Fig. 3. Relation between ophthalmoscopic grouping and certain clinical findings or complications of hypertension. Reproduced by permission of the *Journal of the American Medical Association.*[2]

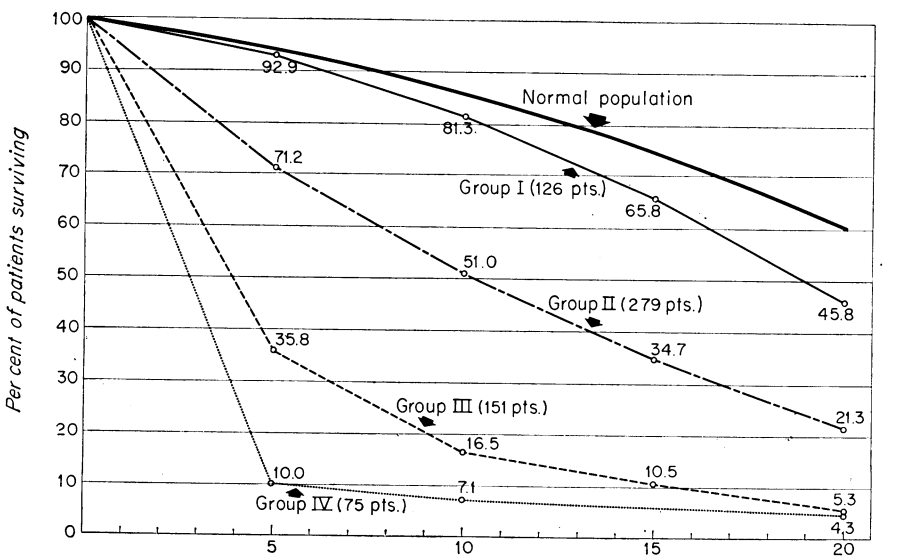

Fig. 4. Survival rates in hypertension of Groups 1 through 4 (Keith-Wagener-Barker classification) for a 20-year period (1940-1960). Reproduced by permission of the American Heart Association, Inc.[10]

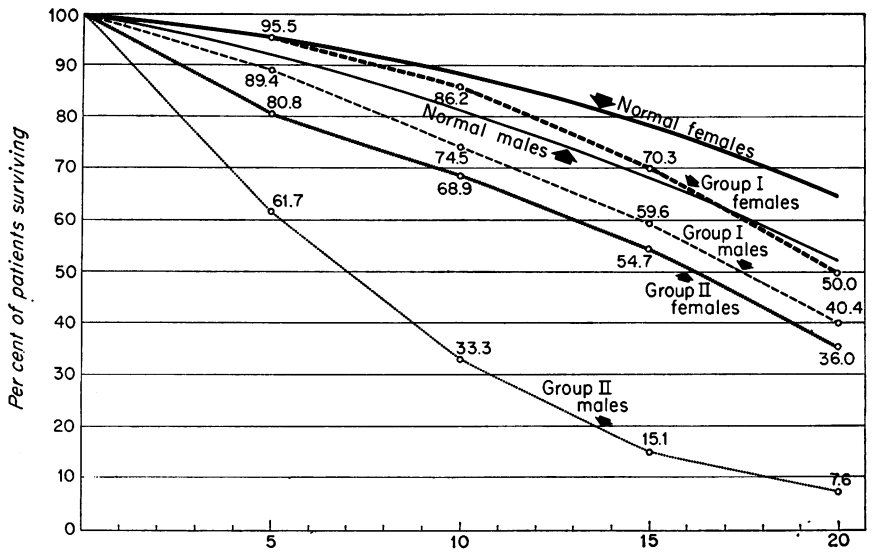

Fig. 5. Survival rates in untreated hypertension Groups 1 and 2 (Keith-Wagener-Barker classification) by sex for a 20-year period (1940-1960). Reproduced by permission of the American Heart Association, Inc.[10]

increased intracranial pressure.[9] Like retinal hemorrhages and exudates, papilledema regularly regresses when blood pressure is reduced.[4, 5]

Ophthalmoscopic Grouping and Prevalence of Hypertensive Complications

It has already been stated that the severity of retinal arteriolar narrowing is a reliable index to the severity of diastolic hypertension. There is also a direct relation between ophthalmoscopic grouping according to the Keith-Wagener-Barker criteria and the prevalence of certain complications of hypertension (Figure 3).

Inverted T waves in lead I were present in the electrocardiograms of 7% of 42 patients with Group 1 hypertension and in 38% of 58 patients with Group 4 hypertension. Of 100 patients with Group 1 hypertension, 9% had cardiomegaly according to roentgenographic measurement, while of 72 patients with Group 4 hypertension 54% had this finding. Of 108 patients with Group 1 hypertension only 13% had proteinuria of grade 2 or more severity, while of 74 patients with Group 4 hypertension 88% had this degree of proteinuria. Of 107 patients with Group 1 hypertension none had azotemia, while of 73 patients with Group 4 hypertension one third had azotemia.[2]

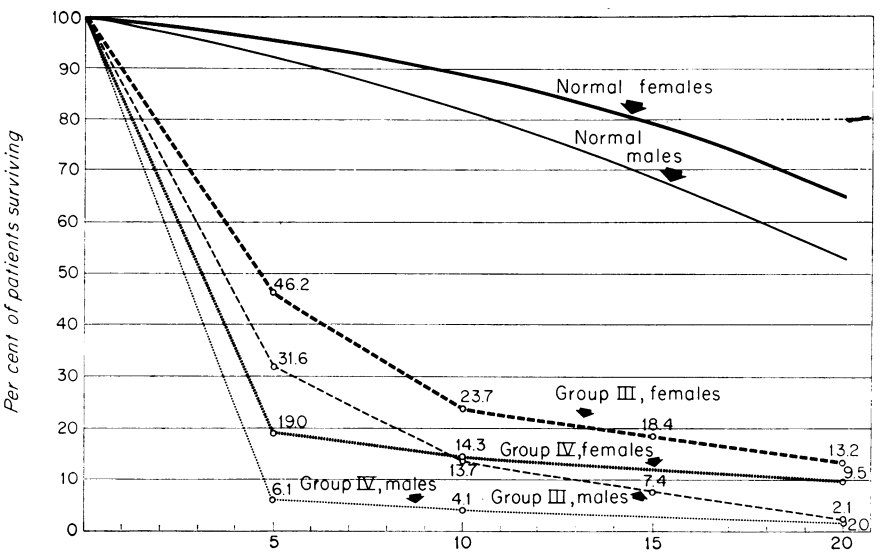

Fig. 6. Survival rates in untreated hypertension of groups 3 and 4 (Keith-Wagener-Barker classification) by sex for a 20-year period (1940-1960). Reproduced by permission of the American Heart Association, Inc.[10]

Ophthalmoscopic Grouping and Survival of Untreated Hypertensive Patients

There is a direct relation between severity of ophthalmoscopic grouping and mortality of untreated hypertensive patients.[1, 2, 10] Even in patients with Group 1 ophthalmoscopic changes, the 10- and 20-year mortality rates were higher than would be expected in a population of similar age range and sex distribution (Figure 4).[10] The 5-year mortality rate for patients with Group 4 (malignant hypertension) was 99% in the series reported by Keith et al.,[1] and 90% in the series reported by Breslin et al.[10] In most reports, the mortality rate for untreated patients with Group 4 hypertension has been 100% in from 5 to 10 years.[9, 11-13]

Within each ophthalmoscopic group the prognosis is worse for men than for women (Figures 5 and 6).[10] The difference is greatest in Group 2, in which the 10-year survival rate for men is one half that for women, while the 20-year survival rate for men is one fifth that for women (Figure 5).

For any specific level of diastolic blood pressure the prognosis worsens from the lower to the higher ophthalmoscopic groups (Table

TABLE II. RELATION OF AVERAGE DIASTOLIC BLOOD PRESSURE TO SURVIVAL OF HYPERTENSIVE PATIENTS

Average diastolic blood pressure, Mm. Hg	*Patients Traced 10 Years or More**					
	Group 1		*Group 2*		*Group 3*	
	No.	*% Surviving*	*No.*	*% Surviving*	*No.*	*% Surviving*
< 100	56	84	77	61	8	25
100-119	47	77	115	51	39	23
120-139	9	89	40	38	57	18
> 139	.....	.....	7	14	29	3

*Group 4 omitted because data were too few to give meaningful percentages.
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TABLE III. RELATION OF SOME NONRETINAL COMPLICATIONS TO SURVIVAL OF HYPERTENSIVE PATIENTS

Nonretinal complications	*Patients Traced 10 Years or More**					
	Group 1		*Group 2*		*Group 3*	
	No.	*% Surviving*	*No.*	*% Surviving*	*No.*	*% Surviving*
None	81	86	39	69	12	42
Cardiomegaly by roentgenography	10	100	46	30	50	16
Inverted T waves in lead 1 in ECG	3	67	14	29	33	6
Angina pectoris	4	50	14	29	4	0
Proteinuria (grade 2 or more)	14	57	52	25	76	4

*Group 4 omitted because data were too few to give meaningful percentages.
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2).[2] In other words, it is better to have a diastolic blood pressure of 115 mm. Hg with Group 1 fundi than to have the same pressure with Group 3 fundi. With the possible exception of Group 1, the prognosis also worsens within each group as the diastolic blood pressure increases. For example, it is better to have Group 2 fundi with a diastolic blood pressure of 100 mm. Hg than to have Group 2 fundi with a diastolic pressure of 135 mm. Hg. Also, it is better to have a diastolic blood pressure in the range of 120 to 139 mm. Hg with Group 2 fundi than a diastolic blood pressure in the range of 100 to 119 mm. Hg with Group 3 fundi.

When complications are absent in hypertensive patients, the only

clue to prognosis is the level of diastolic blood pressure and the appearance of the optic fundi. Table III shows that, in the absence of complications, the ophthalmoscopic classification has definite prognostic value.[2] The data also demonstrate that for at least some complications of hypertension the prognosis worsens from lower to higher ophthalmoscopic groups. Thus the prognosis was better for patients who had cardiomegaly, abnormal electrocardiographic findings, angina pectoris, or proteinuria with Group 1 fundi than it was for those with the same complications with Group 3 fundi.

Diagnostic Value of Ophthalmoscopic Findings

Sometimes clues derived from ophthalmoscopic examination can lead the clinician to suspect or exclude certain secondary causes for hypertension. For instance, Group 4 retinal changes are almost never found in patients with coarctation of the aorta, primary aldosteronism, or unilateral atrophic pyelonephritis; whereas Group 4 neuroretinopathy is frequently associated with hypertension secondary to renal artery disease, pheochromocytoma, and chronic glomerulonephritis. The rapid development of Group 4 neuroretinopathy within 6 months of onset of hypertension is virtually diagnostic of renal vascular hypertension. The finding of mixed diabetic and hypertensive retinal changes provides evidence for diabetic glomerulosclerosis as the cause for hypertension. Cholesterol emboli in the retinal arterioles (Hollenhorst plaques) are indicative of carotid atherosclerosis.[14]

Summary

Careful examination of the optic fundi is an indispensable part of the study of hypertensive patients. It can give valuable clues to the duration, severity, diagnosis, and prognosis of hypertension, as well as to the efficacy of treatment. At the first examination of a hypertensive patient, ophthalmoscopic findings are infinitely more informative than the level of blood pressure. The more severe the hypertension as judged from the optic fundi, the more likely it is that cardiac and renal complications are present, or will occur, and the worse the prognosis for survival without treatment. In the absence of complications, ophthalmoscopic grouping and level of blood pressure are the only guides to prognosis, and even in the presence of most complications, changes in the optic fundi have prognostic significance.

REFERENCES

1. Keith, N. M., Wagener, H. P. and Barker, N. W. Some different types of essential hypertension: Their course and prognosis. *Amer. J. Med. Sci. 197*:332-43, 1939.
2. Breslin, D. J., Gifford, R. W., Jr., Fairbairn, J. F., II, and Kearns, T. P. Prognostic importance of ophthalmoscopic findings in essential hypertension. *J.A.M.A. 195*:335-38, 1966.
3. Wagener, H. P., Clay, G. E., and Gipner, J. F. Classification of retinal lesions in presence of vascular hypertension. *Trans. Amer. Ophthal. Soc. 45*:57-73, 1947.
4. Farmer, R. G., Gifford, R. W., Jr. and Hines, E. A., Jr. Effect of medical treatment of severe hypertension; a follow-up study of 161 patients with group 3 and group 4 hypertension. *Arch. Intern. Med. 112*:118-28, 1963.
5. Kirkendall, W. M., and Armstrong, M. L. Effect of blood pressure reduction on vascular changes in the eye. II. Results after two years, In: *Hypertension: Recent Advances,* Moyer, J. H. and Brest, A. N., eds. Philadelphia, Lea and Febiger, 1961, pp. 624-32.
6. Hodge, J. V. and Dollery, C. T. Retinal soft exudates: A clinical study of colour and fluorescence photography. *Quart. J. Med., n. s. 33*:117-31, 1964.
7. Christensen, L. The nature of the cytoid body, *Trans. Amer. Ophthal. Soc. 56*:451-73, 1958.
8. Wolter, J. R. Pathology of a cotton-wool spot. *Amer. J. Ophthal. 48*:473-85, 1959.
9. Kincaid-Smith, P., McMichael, J. and Murphy, E. A. The clinical course and pathology of hypertension with papilloedema (malignant hypertension). *Quart. J. Med., n.s. 27*:117-53 (Jan.) 1958.
10. Breslin, D. J., Gifford, R. W., Jr. and Fairbairn, J. F., II. Essential hypertension: A twenty-year follow-up study. *Circulation 33*:87-97, 1966.
11. Page, I. H. A clinical study of malignant hypertension. *Ann. Intern. Med. 12*:978-1004, 1939.
12. Bjork, S., Sannerstedt, R., Angervall, G. and Hood, B. Treatment and prognosis in malignant hypertension: Clinical follow-up study of 93 patients on modern medical treatment. *Acta Med. Scand. 166*:175-87, 1960.
13. Hodge, J. V., McQueen, E. G. and Smirk, H. Results of hypotensive therapy in arterial hypertension; based on experience with 497 patients treated and 156 controls, observed for periods one to eight years. *Brit. Med. J. 1*:1-7, 1961.
14. Hollenhorst, R. W. Significance of bright plaques in the retinal arterioles. *J.A.M.A. 178*:23-29, 1961.